VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claims 15, 17 and 26 have been amended as follows.

15. (Amended) A method for eliciting an immune response in a vertebrate subject, said method comprising:

(a) providing a core carrier coated with vector constructs carrying genomic DNA fragments derived or obtained from one or more pathogens, wherein the genomic DNA fragments contain an antigen coding sequence, and are greater than 5 kilobases in size; and

(b) administering the coated core carrier to the subject using a particle-mediated transdermal delivery technique, whereby antigen encoded by a coding sequence present in the genomic DNA fragments is expressed in the subject in an amount sufficient to elicit an immune response.

17. (Amended) The method of claim 15, wherein the vector construct is a plasmid.

26. (Amended) The method of claim 15, wherein the vector construct is a cosmid.

REMARKS

Introductory Comments:

Claims 1-51 are pending in the application. Applicants note with appreciation that the Office has acknowledged applicants' election of Group III, claims 15-25 as provided for in the Response filed 3 January 2002. Applicants also note that Groups I and II have now been combined, as well as Groups III and IV. As a result, applicants' elected group is Group III as now redefined to include claims 15-34. Claims 1-14 and 35-51 have been withdrawn from further consideration pursuant to 37 C.F.R. § 1.142(b) as drawn to a non-elected invention.

Accordingly, claims 15-34 are currently under consideration and were examined in the Office Action dated 5 October 2002. In the Action, the Office has asserted the following claim rejections: **(1)** claims 15-34 stand rejected under 35 U.S.C. § 112, second paragraph, as indefinite; **(2)** claims 15-34 stand rejected under 35 U.S.C.§112, first paragraph, as nonenabled; **(3)** claims 15, 17-19, 22-28 and 31-34 stand rejected under 35 U.S.C. §102(a) as unpatentable over International Publication No. WO 99/31262 to Barry et al. ("Barry"); **(4)** claims 15-19, 22-25 and 31-34 stand rejected under 35 U.S.C. § 102(a) as unpatentable over Braun et al. (1999) *Virology* 265:46-56 ("Braun"); **(5)** claims 15, 17-19, 22-28 and 31-34 stand rejected under 35 U.S.C. §102(a) as unpatentable over Tacket et al. (1999) *Vaccine* 17:2826-2829 ("Tacket"); **(6)** claims 15, 17-19, 22-28 and 31-34 stand rejected under 35 U.S.C. §102(b) as unpatentable over Lodmell et al. (1998) *Vaccine* 16:115-118 ("Lodmell"); **(7)** claims 15, 17-19, 22-28 and 31-34 stand rejected under 35 U.S.C. §102(b) as unpatentable over Haynes et al. (1994) *AIDS Research and Human Retroviruses* 10:S43-S45 ("Haynes"); **(8)** claims15, 17-19, 22-28 and 31-34 stand rejected under 35 U.S.C. §102(b) as unpatentable over Webster et al. (1994) *Vaccine* 12:1495-1498

("Webster"); **(9)** claims 15, 17-19, 22-28 and 31-34 stand rejected under 35 U.S.C. §102(b) as unpatentable over Macklin et al. (1998) *J. Virology* 72:1491-1496 ("Macklin"); **(10)** claims 15, 17-19, 22-28 and 31-34 stand rejected under 35 U.S.C. §102(b) as unpatentable over Fynan et al. (1993) *Proc. Natl. Acad. Sci. USA* 90:11478-11482 ("Fynan"); **(11)** claims 15, 17-19, 22-28 and 31-34 stand rejected under 35 U.S.C. §102(b) as unpatentable over U.S. Patent No. 6,194,389 to Johnston et al. ("Johnston"); and **(12)** claims 15-34 stand rejected under 35 U.S.C. §103(a) as unpatentable over Johnston, Braun, Stanberry et al. (1987) *J. Infect. Dis.* 155:156-163 ("Stanberry"), Pertmer et al. (1995) *Vaccine* 15:1427-1430, and Barry et al. (1997) *Vaccine* 15:788-791 ("Barry2"). Applicants respectfully traverse these rejections for the following reasons.

Overview of the Amendment:

Applicants, by way of this response, have entered minor amendments to claims 15, 17 and 26. In particular, all three claims have been amended to add the word "vector" in front of the word "construct." Support for these amendments can be found throughout the specification as originally filed, for example, at page 13, lines 13-18; page 18, line 14 through page 19, line 7; page 26, lines 5-26; and page 27, lines 7-18. Accordingly, no new matter has been added by way of these claim amendments, and the entry thereof is respectfully requested.

A marked-up version of the changes made to the claims by the current amendment is attached and appears herein above. The attached page is captioned "Version With Markings to Show Changes Made."

The Rejections under 35 U.S.C. §112, second paragraph:

Claim 15 stands rejected under 35 U.S.C. §112, second paragraph, as indefinite. In particular, the Office has objected that the term "construct" is inadequately defined. Clarification was requested.

In response, applicants draw the Office's attention to the amendment to claim 15 wherein "construct" is now recited as "vector construct." Applicants submit that the amendment is sufficient to overcome the Office's objection, and reconsideration and withdrawal of the rejection is thus respectfully requested.

Claim 15 also stands rejected under 35 U.S.C. §112, second paragraph, as indefinite on the basis that the term "derived" does not provide the requisite standard of clarity. Applicants respectfully traverse.

Applicants note that the primary purpose of Section 112's requirement for clarity and precision is to ensure that the public is informed of the metes and bounds of the claimed invention. Applicants also note that definiteness of claim language must be analyzed, not in a vacuum, but in light of (1) the content of the disclosure provided by the specification; (2) the teachings of the prior art; and (3) the claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made.

Applicants respectfully submit that the subject term is indeed clear for the purposes of Section 112, second paragraph. For example, referring to the content of the specification, applicants have provided a clear and concise definition for the phrase "derived from" (see page 15, lines 1-4) and a series of tests for determining if a sequence is "derived from" a particular molecule (see page 15, line 22 through page 17, line 20). The skilled artisan reading applicants' claims would readily understand what "derived from" means in the context of the claim and would be able to confirm this understanding by a brief review of the specification. Accordingly, the rejection of

claim 15 is improper. Reconsideration and withdrawal of the rejection is respectfully requested. Claim 15 has also been objected to on the basis that the open language of "one or more pathogens" fails to define the upper limitation of the recited subject matter. Applicants respectfully traverse.

Claim language must be assessed using a "reasonableness" standard, wherein recited terms are given their broadest "reasonable" interpretation in light of the specification and the understanding of those of ordinary skill in the art. *In re Marosi*, 218 USPQ 289 (Fed. Cir. 1983), (emphasis in original). In the rejection, the Office questions if the claims can include "10 pathogens" (Office Action at page 3). Applicants respectfully submit that the answer is clear. The claims call for the inclusion of genomic fragments of 5 kilobases in size. The ordinarily skilled artisan understands that the upper limit for plasmid vector constructs is about 25 kilobases of guest nucleic acids, and that upper limit for cosmid vector constructs is about 50 kilobases of guest nucleic acids. Exceeding the upper limit for either of these types of constructs results in a highly unstable molecule, and the skilled artisan would not attempt to exceed these limits. Thus, if the vector construct is a plasmid, then the upper limit would be five different pathogens (5X5 = 25), with the skilled artisan tending toward the lower end of the range (typically 5 kilobases molecules from 2 different pathogens for a total of 10 kilobases), whereas if the vector construct is a cosmid, then the upper limit would be ten different pathogens (10X5 = 50). Accordingly, the upper limit is present in the claim in the form of a common sense, "reasonableness" limitation in light of the knowledge possessed by the ordinarily skilled artisan. Accordingly, the rejection of claim 15 is deemed improper, and reconsideration and withdrawal of the rejection is respectfully requested.

Claim 15 further stands rejected under 35 U.S.C. §112, second paragraph, on the basis that "a particle-mediated transdermal technique" is not defined. Applicants respectfully traverse.

In particular, applicants draw the Office's attention to the specification at page 11, lines 2-17 for the express definition of "particle-mediated delivery" and page 19, lines 16-22; page 33, line 25 through page 35, line 12; and page 35, line 16 through page 36, line 1 for additional disclosure about the technique. Accordingly, the rejection of claim 15 is deemed improper. Reconsideration and withdrawal of the rejection is respectfully requested.

Claim 15 also stands rejected under 35 U.S.C. §112, second paragraph, as indefinite on the basis that "an amount sufficient" is not taught by the specification. Applicants respectfully traverse.

In particular, applicants draw the Office's attention to page 36, lines 2-19; page 37, line 23 through page 38, line 1; and page 41, lines 1-20, for express disclosure regard "an amount sufficient" as intended by the claims. Accordingly, the rejection of claim 15 is deemed improper. Reconsideration and withdrawal of the rejection is respectfully requested.

Claims 19 and 28 stand rejected under 35 U.S.C. §112, second paragraph, as indefinite. In particular, the Office has objected to the recitation that the constructs can comprise (genomic fragments) from "at least one pathogen," and submits that since there is no upper limitation, "can 100 pathogens be intended?" Office Action at page 3. Applicants respectfully traverse.

As discussed above, claim language must be assessed using a "reasonableness" standard, wherein recited terms are given their broadest "reasonable" interpretation in light of the specification and the understanding of those of ordinary skill in the art. The claims call for the inclusion of genomic fragments of 5 kilobases in size. The

ordinarily skilled artisan understands that the upper limit for plasmid vector constructs is about 25 kilobases of guest nucleic acids, and that upper limit for cosmid vector constructs is about 50 kilobases of guest nucleic acids. Exceeding the upper limit for either of these types of constructs results in a highly unstable molecule, and the skilled artisan would not attempt to exceed these limits. Thus, if the vector construct is a plasmid, then the upper limit would be five different pathogens (5X5 = 25), with the skilled artisan tending toward the lower end of the range (typically 5 kilobases molecules from 2 different pathogens for a total of 10 kilobases), whereas if the vector construct is a cosmid, then the upper limit would be ten different pathogens (10X5 = 50). Use of 100 different pathogens would result in a vector construct carrying 500 kilobases of quest nucleic acids (5X100 = 500), which is, of course ridiculous. Accordingly, the upper limit is present in the claim in the form of a common sense, "reasonableness" limitation in light of the knowledge possessed by the ordinarily skilled artisan. Accordingly, the rejection of claims 19 and 28 is deemed improper, and reconsideration and withdrawal of the rejection is respectfully requested.

Claims 19 and 28 also stand rejected under 35 U.S.C. §112, second paragraph, as indefinite on the basis that the phrase "the pathogen" does not have proper antecedent basis. Applicants respectfully traverse.

Claims 19 and 28 depend indirectly from claim 15, which recites in part (a) "genomic fragments derived or obtained from one or more pathogens." Since claims 19 and 28 depend indirectly from claim 15, they contain this same limitation. Accordingly, the rejection of claims 19 and 28 is improper. Reconsideration and withdrawal of the rejection is respectfully requested.

Claims 21 and 30 stand rejected under 35 U.S.C. §112, second paragraph, as indefinite on the basis that the phrase "more than one virus" fails to define an upper limitation. Applicants respectfully traverse.

As discussed above, claim language must be assessed using a "reasonableness" standard, wherein recited terms are given their broadest "reasonable" interpretation in light of the specification and the understanding of those of ordinary skill in the art. The claims call for the inclusion of genomic fragments of 5 kilobases in size. The ordinarily skilled artisan understands that the upper limit for plasmid vector constructs is about 25 kilobases of guest nucleic acids, and that upper limit for cosmid vector constructs is about 50 kilobases of guest nucleic acids. Exceeding the upper limit for either of these types of constructs results in a highly unstable molecule, and the skilled artisan would not attempt to exceed these limits. Thus, if the vector construct is a plasmid, then the upper limit would be five different viruses (5X5 = 25), with the skilled artisan tending toward the lower end of the range (typically 5 kilobases molecules from 2 different viruses for a total of 10 kilobases), whereas if the vector construct is a cosmid, then the upper limit would be ten different viruses (10X5 = 50). Accordingly, the upper limit is present in the claim in the form of a common sense, "reasonableness" limitation in light of the knowledge possessed by the ordinarily skilled artisan. Accordingly, the rejection of claims 21 and 30 is deemed improper, and reconsideration and withdrawal of the rejection is respectfully requested.

Claims 22 and 31 stand rejected under 35 U.S.C. §112, second paragraph, as indefinite on the basis that the phrase "a density sufficient" is not defined and not taught by the specification. Office Action at page 4. Applicants respectfully traverse.

In particular, applicants draw the Office's attention to the specification at page 4, lines 1-12; page 11, lines 6-13; and page 38, line 28 through page 40, line 7, where "a sufficient density" is expressly defined and taught. Accordingly, the rejection of claims 22 and 31 is deemed improper, and reconsideration and withdrawal of the rejection is respectfully requested.

Claims 23 and 32 stand rejected under 35 U.S.C. §112, second paragraph, on the basis that the metes and bounds of a "metal" are not defined. Applicants respectfully traverse.

In particular, applicants draw the Office's attention to the specification at page 8, lines 1-7 and page 33, line 22 through page 34, line 14, wherein suitable types of metals are expressly defined and taught. Accordingly, the rejection of claims 23 and 32 is deemed improper, and reconsideration and withdrawal of the rejection is respectfully requested.

The Rejection under 35 U.S.C. §112, first paragraph:

Claims 15-34 stand rejected under 35 U.S.C. §112, first paragraph, as nonenabled. In particular, the Office asserts "the specification, while being enabling for a method for using a DNA-coated gold particle ... carrying ... HSV glycoprotein D to induce an immune response in an animal, does not reasonably provide enablement for [other pathogens]." Office Action at page 4. The Office goes on to assert "the specification does not teach how to select other antigens form any or all pathogenic viruses;" "fails to teach how to construct a plasmid carrying more than one antigens derived from more than one pathogen;" "it is unpredictable whether a DNA-coated particle carrying multiple antigens from multiple pathogenic viruses can induce an immune response; and "undue experimentation would be required for a skilled artisan to make and use the full scope of the invention." Office Action at page 5. Applicants respectfully traverse.

Applicants' burden under Section 112 is merely to provide a specification that enables a person reasonably skilled in the art to make and use the claimed invention without undue experimentation. The fact that some experimentation may be employed, however, does not make it undue if a person of skill in the art typically

engages in such experimentation. This is because the prohibition is against "undue experimentation," not merely "experimentation." *In re Angstadt*, 190 USPQ 214 (CCPA 1976).

With regard to the Office's assertion that the specification is limited exclusively to assembly and use of a plasmid encoding a single HSV gD antigen, applicants wish to draw the Office's attention to the Examples (pages 41-49) where numerous different antigen constructs have been assembled according to the claimed invention and then demonstrated to have the recited features in working, art-recognized animal model systems. In Example 1, six different cosmid constructs were made, each containing different EcoR1 restriction genomic fragments from HSV2, and these were administered to mice in an art-recognized model and established to induce the desired immune response. In Example 2, a plasmid construct was made containing 8500 bp of HSV-2 DNA (including genomic sequences encoding glycoprotein B protein antigen) and this construct was administered to mice in an art-recognized model and established to induce the desired immune response. Accordingly, the premise for the Office's rejection is incorrect.

With respect to the Office's contention that applicants' working models with the various HSV genomic fragments would not provide sufficient guidance for other antigens systems from other pathogens, applicants respectfully disagree. Applicants have provided a detailed disclosure of antigen-encoding sequences that are to be used in the practice of the invention, where to find the sequence information for such antigens, how to go about obtaining the sequences, how to select appropriate control sequences, how to produce an expression cassette, how to insert the expression cassettes into numerous different vector constructs, and how to administer these various vector constructs to obtain expression of the antigens of interest. Although not required under Section 112 (*In re Robbins*, 166 U.S.P.Q. 552 (CCPA 1970)),

applicants have exemplified their thoroughly enabling disclosure with a number of working examples using art-recognized animal model systems.

In addition, the Office itself has admitted that "because the method for using the gene gun for delivering a DNA-coated particle loaded with a DNA plasmid for inducing an immune response is well established method with more efficient effect and economic benefit, the modification of the plasmid carrying more than one antigens either from the same pathogenic virus or from different pathogenic viruses is generally recognized as being within the level of the ordinary skill in the art, since most available antigens used in the art are all well characterized [and] discovering the workable ranges involves only routine skill in the art." Citing *In re Aller*, 105 USPQ 233. See Office Action at page 12, emphasis added. Accordingly, the Office's assertion that the skilled artisan cannot move from applicants' working examples to different antigen systems from different pathogens or even multiple different pathogens is clearly incorrect.

If the Office is suggesting that, absent yet further working examples, applicants' specification cannot be enabling throughout the scope of the claims, such a requirement is improper and not supported by any statutory rule. This is because were such a requirement actually valid, it would discourage inventors from disclosing and teaching their discoveries for the public's benefit until an exhaustive experimental study into any and all possible embodiments had been completed, which discouragement is antithetical and in direct contradiction of the guiding principals underlying Section 112. See, e.g., *Rohm & Hass Co. v. Dawson Chemical Co.*, 217 USPQ 515, 563-564 (S.D. Tex. 1983), *rev'd on other grounds*, 220 USPQ 289 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984).

Applicants have shown that their invention is fully operative across a wide variety of different constructs. There is frankly no valid reason to doubt that

applicant's compositions will be entirely suitable for use with other pathogens, or with multiple pathogens. The Office has thus failed in its burden to provide a reasonable basis to question the enablement that applicant has provided *In re Wright*, 27 USPQ2d 1510 (Fed. Cir. 1993). In fact, the only way to supplant applicants' presumptively correct disclosure (supported by multiple working examples) is to completely ignore or discount the experimental showing that applicants have provided. This is improper since applicants' disclosure must be viewed as in compliance with the enablement requirement of Section 112, unless there is reason to doubt the objective truth thereof. *In re Marzocchi*, 169 USPQ 367 (CCPA 1971).

With regard to the Offices objection that "it would have required undue experimentation to practice the invention as claimed," applicants note that the determination of whether or not something is indeed undue experimentation must be judged by the standards of those skilled in the art. Applicants submit that, given the level of skill in the art which is generally acknowledged to be high in the fields of immunology and molecular biology, the detailed description provided by the specification, and the numerous working examples, a skilled artisan could readily practice the claimed invention without undue experimentation. See, e.g., *Utter v. Hiraga*, 6 USPQ2d 1709, 1714 (Fed. Cir.1988), and *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81, 94 (Fed. Cir. 1986).

Applicants have provided more than sufficient disclosure regarding how to make and use their recited compositions, and have exemplified this disclosure with express working examples. The skilled artisan would thus have no difficulty in following applicants' directions to test other compositions for their ability to produce an immune response in a suitable subject. Although some experimentation may need to be carried out, the mere fact that some experimentation may be required to practice the invention throughout its entire scope does not necessarily make it "undue,"

particularly when the level of skill in the art is typically high, and such experimentation is routinely carried out. It is well settled that satisfaction of the enablement requirement of Section 112 is not precluded by the necessity for some experimentation such as routine screening.

Accordingly, the rejection of claims 15-34 under 35 U.S.C. §112, first paragraph, is improper and simply not supported by any evidence of record in the case. Reconsideration and withdrawal of the rejection is thus earnestly solicited.

The Rejections under 35 U.S.C. §102(b):

Claims 15, 17-19, 22-28 and 31-34 stand rejected under 35 U.S.C. §102(a) as anticipated by Barry. In particular, the Office asserts that Barry et al. "disclose a method for delivering nucleic acid molecule into a mammal .... the nucleic acid sequence encodes an antigenic protein including viral antigen ... and is packaged as a gold particle ... [and] they disclose that the method results in an antibody response." The Office then concludes "the claimed invention is anticipated by the cited reference." Office Action at page 5. Applicants respectfully traverse the rejection.

Anticipation of a claim under §102 *requires* that each and every element of the claims be inherent in, or disclosed expressly by the anticipating reference. *Constant v. Advanced Micro-Devices, Inc.*, 7 USPQ2d 1057, 1064 (Fed. Cir. 1988). Exclusion of a single claimed element from a prior art reference is enough to negate anticipation by that reference. *Atlas Powder Co. v E.I. du Pont De Nemours & Co.* 224 USPQ 409, 411 (Fed. Cir. 1984). Further, anticipation basically requires identity with the prior art document (*Tyler Refrigeration v. Kysor Indus. Corp.*, 227 USPQ 845 (Fed. Cir. 1985)), where the identical invention must be shown in as complete detail as is contained in the rejected claim (*Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913 (Fed. Cir. 1989)). Finally, in order to anticipate, a prior art

reference must be enabling, thus placing the allegedly disclosed matter in the possession of the public. *Akzo N.V. v. United States ITC*, 1 USPQ2d 1241 (Fed. Cir. 1986).

Barry clearly fails to anticipate applicants' recited invention since it fails to provide any disclosure whatsoever regarding applicants' recited methods which require that vector constructs containing genomic fragments "greater than 5 kilobases in size" are administered to produce an immune response. Barry fails to disclose a construct containing a ≥5 kilobase genomic fragment. Since Barry does not disclose applicants' particularly recited constructs, it does not disclose each and every element of the claims as required under Section 102, and thus fails to anticipate applicants' invention. For theses reasons, then, the rejection of claims15, 17-19, 22-28 and 31-34 under 35 U.S.C. §102(a) is improper. Reconsideration and withdrawal of the rejection is thus respectfully requested.

Claims 15, 17-19, 22-28 and 31-34 stand rejected under 35 U.S.C. §102(a) as anticipated by Braun. In particular, the Office asserts that Braun et al. "disclose a method of gold particle-mediated DNA immunization, wherein the DNA sequence encodes a glycoprotein D of Bovine herpesvirus-1 antigen;" and concludes "the claimed invention is anticipated by the cited reference." Office Action at page 6. Applicants respectfully traverse the rejection.

Braun clearly fails to anticipate applicants' recited invention since it fails to provide any disclosure whatsoever regarding applicants' recited methods which require that vector constructs containing genomic fragments "greater than 5 kilobases in size" are administered to produce an immune response. Braun fails to disclose a construct containing a ≥5 kilobase genomic fragment. Since Braun does not disclose applicants' particularly recited

constructs, it does not disclose each and every element of the claims as required under Section 102, and thus fails to anticipate applicants' invention. For theses reasons, then, the rejection of claims15, 17-19, 22-28 and 31-34 under 35 U.S.C. §102(a) is improper. Reconsideration and withdrawal of the rejection is thus respectfully requested.

Claims 15, 17-19, 22-28 and 31-34 stand rejected under 35 U.S.C. §102(a) as anticipated by Tacket. In particular, the Office asserts that Tacket et al. "disclose a method for gold particle-mediated DNA immunization, wherein the DNA sequence encodes a hepatitis-B surface antigen (HBsAg) ... delivered by the PowderJect XR1 particle acceleration device ... to induce a booster response against HBsAg;" and concludes "the claimed invention is anticipated by the cited reference. Office Action at page 6. Applicants respectfully traverse the rejection.

Tacket clearly fails to anticipate applicants' recited invention since it fails to provide any disclosure whatsoever regarding applicants' recited methods which require that vector constructs containing genomic fragments "greater than 5 kilobases in size" are administered to produce an immune response. Tacket fails to disclose a construct containing a ≥5 kilobase genomic fragment. Since Tacket does not disclose applicants' particularly recited constructs, it does not disclose each and every element of the claims as required under Section 102, and thus fails to anticipate applicants' invention. For theses reasons, then, the rejection of claims15, 17-19, 22-28 and 31-34 under 35 U.S.C. §102(a) is improper. Reconsideration and withdrawal of the rejection is thus respectfully requested.

Claims 15, 17-19, 22-28 and 31-34 stand rejected under 35 U.S.C. §102(b) as anticipated by Lodmell. In particular, the Office asserts that Lodmell et al. "disclose a method for using a gene gun for delivering a particle-mediated vaccine comprising DNA encoding glycoprotein (G) gene of rabies virus packaged as ... gold powder ... to

produce long term protective immunity;" and concludes "the claimed invention is anticipated by the cited reference. Office Action at page 7. Applicants respectfully traverse the rejection.

Lodmell clearly fails to anticipate applicants' recited invention since it fails to provide any disclosure whatsoever regarding applicants' recited methods which require that vector constructs containing genomic fragments "greater than 5 kilobases in size" are administered to produce an immune response. Lodmell fails to disclose a construct containing a ≥5 kilobase genomic fragment. Since Lodmell does not disclose applicants' particularly recited constructs, it does not disclose each and every element of the claims as required under Section 102, and thus fails to anticipate applicants' invention. For theses reasons, then, the rejection of claims 15, 17-19, 22-28 and 31-34 under 35 U.S.C. §102(b) is improper. Reconsideration and withdrawal of the rejection is thus respectfully requested.

Claims 15, 17-19, 22-28 and 31-34 stand rejected under 35 U.S.C. §102(b) as anticipated by Haynes. In particular, the Office asserts that Haynes et al. "disclose a method for using ... particle-mediated gene delivery for delivering a DNA vaccine, wherein the plasmid DNA-coated gold microparticles encode the HIV gp160 and gp 120 expression construct ... [and] stimulated the induction of antigen-specific humoral and cytotoxic cellular immune response;" and then concludes "the claimed invention is anticipated by the cited prior art." Office Action at page 7. Applicants respectfully traverse the rejection.

Haynes clearly fails to anticipate applicants' recited invention since it fails to provide any disclosure whatsoever regarding applicants' recited methods which require that vector constructs containing genomic fragments "greater than 5 kilobases in size" are administered to produce an immune response. Haynes fails to disclose a construct containing a ≥5 kilobase genomic fragment. Since Haynes does

not disclose applicants' particularly recited constructs, it does not disclose each and every element of the claims as required under Section 102, and thus fails to anticipate applicants' invention. For theses reasons, then, the rejection of claims15, 17-19, 22-28 and 31-34 under 35 U.S.C. §102(b) is improper. Reconsideration and withdrawal of the rejection is thus respectfully requested.

Claims 15, 17-19, 22-28 and 31-34 stand rejected under 35 U.S.C. §102(b) as anticipated by Webster. In particular, the Office asserts that Webster et al. "disclose a method for using [a] particle bombardment device for delivering a DNA vaccine, wherein the plasmid DNA is constructed with cytokine IL-2 ... expresses an influenza virus haemagglutinin ... and provides complete protection immunity;" and then concludes "the claimed invention is anticipated by the cited prior art." Office Action at page 7. Applicants respectfully traverse the rejection.

Webster clearly fails to anticipate applicants' recited invention since it fails to provide any disclosure whatsoever regarding applicants' recited methods which require that vector constructs containing genomic fragments "greater than 5 kilobases in size" are administered to produce an immune response. Webster fails to disclose a construct containing a ≥5 kilobase genomic fragment. Since Webster does not disclose applicants' particularly recited constructs, it does not disclose each and every element of the claims as required under Section 102, and thus fails to anticipate applicants' invention. For theses reasons, then, the rejection of claims15, 17-19, 22-28 and 31-34 under 35 U.S.C. §102(b) is improper. Reconsideration and withdrawal of the rejection is thus respectfully requested.

Claims 15, 17-19, 22-28 and 31-34 stand rejected under 35 U.S.C. §102(b) as anticipated by Macklin. In particular, the Office asserts that Macklin et al. "disclose a method for using [a] particle bombardment device for delivering DNA-coated gold particle carrying the DNA sequence encoding the influenza virus HA protein to induce

an immune response;" and then concludes "the claimed invention is anticipated by the cited reference." Office Action at page 8. Applicants respectfully traverse the rejection.

Macklin clearly fails to anticipate applicants' recited invention since it fails to provide any disclosure whatsoever regarding applicants' recited methods which require that vector constructs containing genomic fragments "greater than 5 kilobases in size" are administered to produce an immune response. Macklin fails to disclose a construct containing a ≥5 kilobase genomic fragment. Since Macklin does not disclose applicants' particularly recited constructs, it does not disclose each and every element of the claims as required under Section 102, and thus fails to anticipate applicants' invention. For theses reasons, then, the rejection of claims15, 17-19, 22-28 and 31-34 under 35 U.S.C. §102(b) is improper. Reconsideration and withdrawal of the rejection is thus respectfully requested.

Claims 15, 17-19, 22-28 and 31-34 stand rejected under 35 U.S.C. §102(b) as anticipated by Fynan. In particular, the Office asserts that Fynan et al. "disclose a method for ... delivering a DNA-coated gold particle carrying the DNA sequence encoding the influenza HA1 or 7 protein ... to induce an immune response;" and then concludes "the claimed invention is anticipated by the cited reference." Office Action at page 8. Applicants respectfully traverse the rejection.

Fynan clearly fails to anticipate applicants' recited invention since it fails to provide any disclosure whatsoever regarding applicants' recited methods which require that vector constructs containing genomic fragments "greater than 5 kilobases in size" are administered to produce an immune response. Fynan fails to disclose a construct containing a ≥5 kilobase genomic fragment. Since Fynan does not disclose applicants' particularly recited constructs, it does not disclose each and every element of the claims as required under Section 102, and thus fails to

anticipate applicants' invention. For theses reasons, then, the rejection of claims15, 17-19, 22-28 and 31-34 under 35 U.S.C. §102(b) is improper. Reconsideration and withdrawal of the rejection is thus respectfully requested.

Claims 15, 17-19, 22-28 and 31-34 stand rejected under 35 U.S.C. §102(b) as anticipated by Johnston. Although section 102(b) has been asserted, applicants assume that the instant rejection is intended under 35 U.S.C. §102(e) since Johnston did not grant until after applicants' filing date. Nevertheless, the Office asserts that Johnston et al. "disclose a method for transferring a gene to vertebrate cells comprising the injection of microprojectiles into the host to induce protective immunity, wherein the microprojectile is a DNA-coated particle carrying a recombinant construct of a gene and a regulatory element. The construct may take any suitable form, such as a plasmid, a genomic viral DNA sequence;" and then concludes "the claimed invention is anticipated by the cited reference." Office Action at page 9. Applicants respectfully traverse the rejection.

Johnston clearly fails to anticipate applicants' recited invention since it fails to provide any disclosure whatsoever regarding applicants' recited methods which require that vector constructs containing genomic fragments "greater than 5 kilobases in size" are administered to produce an immune response. Johnston fails to disclose a construct containing a ≥5 kilobase genomic fragment. Since Johnston does not disclose applicants' particularly recited constructs, it does not disclose each and every element of the claims as required under Section 102, and thus fails to anticipate applicants' invention. For theses reasons, then, the rejection of claims15, 17-19, 22-28 and 31-34 under 35 U.S.C. §102(b)(and/or 102(e)) is improper. Reconsideration and withdrawal of the rejection is thus respectfully requested.

The Rejection under 35 U.S.C. §103(a):

Claims 15-34 stand rejected under 35 U.S.C. §103(a) as unpatentable over Johnston, Braun, Stanberry, Pertmer, and Barry2. In particular, the Office asserts that the various cited references disclose methods for administering DNA vaccine compositions using particle-mediated delivery apparatus (Office Action at pages 10-12), and then concludes "[b]ecause the method for using the gene gun for delivering a DNA-coated particle loaded with a DNA plasmid for inducing an immune response is well established method with more efficient effect and economic benefit, the modification of the plasmid carrying more than one antigens either from the same pathogenic virus or from different pathogenic viruses is generally recognized as being within the level of the ordinary skill in the art, since most available antigens used in the art are all well characterized [and] discovering the workable ranges involves only routine skill in the art." Office Action at page 12. Applicants respectfully traverse the rejection.

Section 2143 of the M.P.E.P. sets forth the following three basic requirements for *prima facie* obviousness: (1) there must be some suggestion or motivation to modify the reference(s); (2) there must be a reasonable expectation of success for the modification; and (3) the prior art reference(s) must teach or suggest all the claim limitations. When assessing these issues, (1) the claimed invention must be considered as a whole; (2) the reference must be considered as a whole and must suggest the desirability of making the modification; (3) the reference must be viewed without the benefit of impermissible hindsight; and (4) a reasonable expectation of success is the standard with which obviousness is determined. *Hodosh v. Block Drug Co., Inc.*, 229 USPQ 182, 187, n.5 (Fed. Cir. 1986). Applicants submit that the Office has failed to satisfy these criteria, and has thus

failed to establish *prima facie* obviousness over its proposed combination of Johnston, Braun, Stanberry, Pertmer, and Barry2.

Johnston, Braun, Stanberry, Pertmer, and Barry2 all fail to teach or even so much as suggest that vector constructs containing genomic fragments "greater than 5 kilobases in size" are administered to produce an immune response. Johnston, Braun, Stanberry, Pertmer, and Barry2 all fail to teach or even so much as suggest a construct containing a ≥5 kilobase genomic fragment. In other words, all of the cited references fail to teach or suggest all of applicants' claim limitations. Since Johnston, Braun, Stanberry, Pertmer, and Barry2 all fail to teach or suggest applicants' particularly recited constructs, no conceivable combination of these references can provide this missing critical element.

Accordingly, when Johnston, Braun, Stanberry, Pertmer, and Barry2 are considered fairly and as a whole, it is clear that they fail to teach or suggest all of the claim limitations, and they also fail to teach or suggest the desirability of making any modification that would produce applicants' recited compositions. Since there is no teaching of suggestion or motivation to modify the references, there cannot have been a reasonable expectation of success for the modification. Thus, the Office has failed to establish its showing of *prima facie* obviousness, and the rejection is improper. Reconsideration and withdrawal of the rejection of claims 15-34 under 35 U.S.C. §103(a) over the combination of Johnston, Braun, Stanberry, Pertmer, and Barry2 is respectfully requested.

CONCLUSION

Applicants respectfully submit that the claims as now pending define an invention which complies with the requirements of 35 U.S.C. § 112 and which is novel and nonobvious over the art. Accordingly, allowance is believed to be in order and an early notification to that effect is earnestly solicited. Applicants further ask that, should the Examiner note any minor remaining issues that may be resolved with a telephone call, that the Examiner contact the undersigned in the UK at +44 1865 332 600.

Respectfully submitted,

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By: _____
Thomas P. McCracken
Registration No. 38,548

POWDERJECT PHARMACEUTICALS PLC
Florey House
The Oxford Science Park
Oxford OX4 4GA
United Kingdom
Telephone: +44 1865 332 600
Fax: +44 1865 332 601